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[Continued on next page]

(54) Title: ADP-RIBOSYLATING TOXIN FROM LISTERIA MONOCYTOGENES

E. coli LT	KLYRADSRPPD	LYDHARGTQ	YDDGYWSTSESERSA	SPHPYEQEVSA LGGI
N. meningitidis	FLYRGTSQOOD	VYAHQIETG	YDGGYSTTQKELA	PENENEKEVTIRAED
S. coelicolor	TYRSDSRGPQVVFEEGFHAKDVONGQYDVEKYVLNQPSPYVSTSYDHDEY			HKWADQVEVAFPGGI
M. pneumoniae	LYRVDLRSPE	PFEHILSTN	GRSYETSTETPTAA	TSEFAYQREWFDTGPI
S. typhi	FLYRVSTPPD		SCSGGSSdSRYIATT	TMMRLQREYVSTLSI
S. paratyphi	FLYRVSTPPD		SCSGGSSdSRYIATT	TMMRLQREYVSTLSI
S. pyogenes	VYRVVETFL		TKHSEFSTALKNGA	SAVPSEVELLFPRGC
L. monocytogenes	ILYRGTSSEIL		EEKGFMSTTTISNOT	SETPLEAEVLFNIGQ

(57) Abstract: An ADP-ribosylating toxin from *Listeria monocytogenes* is disclosed, together with mutant toxins and uses therefor. There is only a low level of sequence identity between this toxin and known toxins such as the iota toxin from *Clostridium perfringens*.

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*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

## INTERNATIONAL SEARCH REPORT

IB2004/001440

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/195 A61K39/02 C12N15/31 C07K16/12

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, WPI Data, PAJ, Sequence Search

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indications, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE UNIPROT 1 March 2002 (2002-03-01), GALSER ET AL: XP002296863 retrieved from EBI Database accession no. Q8YAQ1 abstract -&amp; GLASER P ET AL: "Comparative genomics of listeria species" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 294, no. 5543, 26 October 2001 (2001-10-26), pages 849-852, XP002967927 ISSN: 0036-8075</p> <p style="text-align: center;">----- -/-</p>	<p>1-3,5,6, 8-11, 18-23</p>

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
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- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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- \*G\* document member of the same patent family

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE GSP 18 October 2001 (2001-10-18), BUCHRIESER ET AL: XP002296864 retrieved from EBI Database accession no. ABB48216 abstract	1-3,5,6, 8-11, 18-23
X	-& WO 01/77335 A (PASTEUR INSTITUT) 18 October 2001 (2001-10-18)  abstract; claim 6; sequence 921 page 89, lines 23,24	1-3,5,6, 8-11, 13-15, 17-28
A	EP 0 869 181 A (BIOCINE SPA) 7 October 1998 (1998-10-07) abstract	1-6,8-28

# INTERNATIONAL SEARCH REPORT

ational application No.  
PCT/IB2004/001440

## Box II Observations where certain claims were found unsearchable (Continuation of Item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 2-6(all partially)  
because they relate to subject matter not required to be searched by this Authority, namely:  
Although claim 28 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound.
2. ☒ Claims Nos.: 2-6(all partially)  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of Item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-6 (all complete), 8-28 (all partially)

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

Continuation of Box II.1

Although claim 28 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound.

Continuation of Box II.2

Claims Nos.: 2-6(all partially)

Present claims 2,3,5 and 6 relate to an extremely large number of possible mutated proteins. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the mutated proteins claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Present claim 4 relates to mutated proteins defined by reference to a desirable characteristic or property, namely showing reduced or eliminated ADP-ribosylating activity of the protein. The claim covers all mutated proteins having this characteristic or property, whereas the application provides no support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for such mutated proteins having the claimed characteristic. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the mutated proteins by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

## INTERNATIONAL SEARCH REPORT

IB2004/001440

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0177335	A	18-10-2001	AU 5485701 A CA 2404988 A1 EP 1278853 A2 WO 0177335 A2 JP 2004507217 T	23-10-2001 18-10-2001 29-01-2003 18-10-2001 11-03-2004
EP 0869181	A	07-10-1998	IT 1253009 B EP 0869181 A1 AT 177145 T AT 277183 T AU 3347693 A CA 2127091 A1 DE 69228563 D1 DE 69228563 T2 DE 69233417 D1 DK 620850 T3 WO 9313202 A1 EP 0620850 A1 ES 2127808 T3 GR 3029556 T3 JP 7506240 T JP 3394774 B2 JP 2003000287 A MX 9207685 A1 SG 48217 A1 SG 93200 A1 US 2004137017 A1 US 2002044939 A1 US 6149919 A	10-07-1995 07-10-1998 15-03-1999 15-10-2004 28-07-1993 08-07-1993 08-04-1999 29-07-1999 28-10-2004 27-09-1999 08-07-1993 26-10-1994 01-05-1999 30-06-1999 13-07-1995 07-04-2003 07-01-2003 31-05-1994 17-04-1998 17-12-2002 15-07-2004 18-04-2002 21-11-2000